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CLAIMS

1. A synthetic nucleic acid sequence comprising a non-naturally occurring polymer of nucleic acids that has no more than 95% homology to a naturally occurring nucleic acid sequence which encodes a first protein having an amino acid sequence, wherein the synthetic nucleic acid sequence encodes a second protein having an amino acid sequence, the second protein's amino acid sequence being at least 90% homologous to the amino acid sequence of the first protein, and further wherein the synthetic nucleic acid's sequence has a predicted free energy of folding per base that is at least 4% greater than the predicted free energy of folding per base of the naturally occurring nucleic acid sequence.

2. The synthetic nucleic acid sequence of claim 1 wherein the synthetic sequence has no more than 90% homology to the naturally occurring sequence and the second protein is at least 95% homologous to the first protein, and further wherein the free energy of folding per base of the synthetic sequence is at least 10% greater than the free energy of folding per base of the naturally occurring sequence.

3. The synthetic nucleic acid sequence of claim 1 wherein the synthetic sequence has no more than 85% homology to the naturally occurring sequence and the second protein is at least 97% homologous to the first protein, and further wherein the free energy of folding per base of the synthetic sequence is at least 15% greater than the free energy of folding per base of the naturally occurring sequence.

4. The synthetic nucleic acid sequence of claim 1 wherein the synthetic sequence has no more than 80% homology to the naturally occurring sequence and the second protein is at least 99% homologous to the first protein, and further wherein the free energy of folding per base of the synthetic sequence is at least 20% greater than the free energy of folding per base of the naturally occurring sequence.

5. The synthetic nucleic acid sequence of claim 4 wherein the free energy of folding per base of the synthetic sequence is at least 30% greater than the free energy of folding per base of the naturally occurring sequence.

6. The synthetic nucleic acid sequence of claim 4 wherein the free energy of folding per base of the synthetic sequence is at least 40% greater than the free energy of folding per base of the naturally occurring sequence.

7. The synthetic nucleic acid sequence of claim 1 wherein the free energy of folding per base of the synthetic sequence is at least 10% greater than the free energy of folding per base of the naturally occurring sequence.

8. The synthetic nucleic acid sequence of claim 1 wherein the free energy of folding per base of the synthetic sequence is at least 20% greater than the free energy of folding per base of the naturally occurring sequence.

9. The synthetic nucleic acid sequence of claim 1 wherein the free energy of folding per base of the synthetic sequence is at least 30% greater than the free energy of folding per base of the naturally occurring sequence.

10. The synthetic nucleic acid sequence of claim 1 wherein the free energy of folding per base of the synthetic sequence is at least 40% greater than the free energy of folding per base of the naturally occurring sequence.

11. The synthetic nucleic acid sequence of claim 1 wherein the second protein is an oxidoreductase.

12. The synthetic nucleic acid sequence of claim 11 wherein the oxidoreductase is a flavin oxidase.

13. The synthetic nucleic acid sequence of claim 12 wherein the flavin oxidase is a vanillyl alcohol oxidase.

14. The synthetic nucleic acid sequence of claim 12 wherein the flavin oxidase is a galactose oxidase.

15. The synthetic nucleic acid sequence of claim 11 wherein the oxidoreductase requires a nicotinamide cofactor.

16. The synthetic nucleic acid sequence of claim 1 wherein the second protein is a keto reductase.

17. The synthetic nucleic acid sequence of claim 1 wherein the second protein is a decarboxylase.

18. The synthetic nucleic acid sequence of claim 17 wherein the decarboxylase is an aromatic amino acid decarboxylase.

19. The synthetic nucleic acid sequence of claim 1 wherein the second protein is a synthase.

20. The synthetic nucleic acid sequence of claim 19 wherein the synthase is a myo-inositol phosphate synthase.

21. The synthetic nucleic acid sequence of claim 1 wherein the second protein is a hydantoinase.

22. The synthetic nucleic acid sequence of claim 1 wherein the second protein is a lyase.

23. The synthetic nucleic acid sequence of claim 1 wherein the amino acid sequence of the second protein comprises one of SEQ. ID NO. 32, SEQ. ID NO. 35, SEQ. ID NO. 37, SEQ. ID NO. 39, SEQ. ID NO. 42, SEQ. ID NO. 44, SEQ. ID NO. 46, SEQ. ID NO. 48, SEQ. ID NO. 50, and SEQ. ID NO. 52, SEQ. ID NO. 56, SEQ. ID NO. 60, SEQ. ID NO. 64, SEQ. ID NO. 68, SEQ. ID NO. 75, SEQ. ID NO. 79, SEQ. ID NO. 54, SEQ. ID NO. 58, SEQ. ID NO. 62, SEQ. ID NO. 66, SEQ. ID NO. 70, SEQ. ID NO. 73, and SEQ. ID NO. 77.

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24. The synthetic nucleic acid sequence of claim 1 wherein the amino acid sequence of the second protein comprises one of SEQ. ID NO. 37, SEQ. ID NO. 44, SEQ. ID NO. 48, SEQ. ID NO. 52, SEQ. ID NO. 56, SEQ. ID NO. 60, SEQ. ID NO. 64, SEQ. ID NO. 68, SEQ. ID NO. 75, and SEQ. ID NO. 79.

25. The synthetic nucleic acid sequence of claim 1 wherein the amino acid sequence of the first protein comprises one of SEQ. ID NO. 32, SEQ. ID NO. 35, SEQ. ID NO. 39, SEQ. ID NO. 42, SEQ. ID NO. 46, SEQ. ID NO. 50, SEQ. ID NO. 54, SEQ. ID NO. 58, SEQ. ID NO. 62, SEQ. ID NO. 66, SEQ. ID NO. 70, SEQ. ID NO. 73, and SEQ. ID NO. 77; and the amino acid sequence of the second protein comprises one of SEQ. ID NO. 37, SEQ. ID NO. 44, SEQ. ID NO. 48, SEQ. ID NO. 52, SEQ. ID NO. 56, SEQ. ID NO. 60, SEQ. ID NO. 64, SEQ. ID NO. 68, SEQ. ID NO. 75, and SEQ. ID NO. 79.

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26. A synthetic oligonucleotide having a sequence selected from the group comprising SEQ. ID NO. 33, SEQ. ID NO.36, SEQ. ID NO. 40, SEQ. ID NO. 43, SEQ. ID NO. 51, SEQ. ID NO. 55, SEQ. ID NO. 59, SEQ. ID NO. 63, SEQ. ID NO. 67, SEQ. ID NO. 71, SEQ. ID NO. 74, SEQ. ID NO. 78 and their complementary sequences.

27. The synthetic nucleic acid sequence of claim 1 wherein the difference in free energy of folding per base between the synthetic sequence and the naturally occurring sequence is at least 0.0005 kcal/mol·base.

28. The synthetic nucleic acid sequence of claim 1 wherein the difference in free energy of folding per base between the synthetic sequence and the naturally occurring sequence is at least 0.001 kcal/mol·base.

29. The synthetic sequence of claim 1 wherein the free energy of folding of the synthetic nucleic acid sequence is more positive than about -0.2 kcal/(mol)(base).

30. A first nucleic acid sequence designed to encode the same amino acid sequence as a second nucleic acid sequence, wherein the first nucleic acid sequence has a predicted free energy of folding per base at least about 5% different from the second nucleic acid sequence.

31. The first nucleic acid sequence of claim 30 wherein the difference between the free energies of folding per base is at least about 10%.

32. The first nucleic acid sequence of claim 31 wherein the amino acid sequence is an oxidoreductase.

33. The first nucleic acid sequence of claim 32 wherein the oxidoreductase is a flavin oxidase.

34. The first nucleic acid sequence of claim 33 wherein the flavin oxidase is a vanillyl alcohol oxidase.

35. The first nucleic acid sequence of claim 33 wherein the flavin oxidase is a galactose oxidase.

36. The first nucleic acid sequence of claim 32 wherein the oxidoreductase requires a nicotinamide cofactor.

37. The first nucleic acid sequence of claim 31 wherein the amino acid sequence is a keto reductase.

38. The first nucleic acid sequence of claim 31 wherein the amino acid sequence is a decarboxylase.

39. The first nucleic acid sequence of claim 38 wherein the decarboxylase is an aromatic amino acid decarboxylase.

40. The first nucleic acid sequence of claim 31 wherein the amino acid sequence is a synthase.

41. The first nucleic acid sequence of claim 40 wherein the synthase is a myo-inositol phosphate synthase.

42. The first nucleic acid sequence of claim 31 wherein the amino acid sequence is a hydantoinase.

43. The first nucleic acid sequence of claim 31 wherein the amino acid sequence is a lyase.

44. The first nucleic acid sequence of claim 30 wherein the difference between the free energies of folding per base is at least about 20%.

45. The first nucleic acid sequence of claim 30 wherein the difference between the free energies of folding per base is at least about 30%.

46. The first nucleic acid sequence of claim 30 wherein the difference between the free energies of folding per base is at least about 40%.

47. The first nucleic acid sequence of claim 31 wherein the predicted free energy of folding per base is greater than that of the second nucleic acid sequence.

48. The first nucleic acid sequence of claim 31 wherein the second nucleic acid sequence is a naturally-occurring sequence.

49. The first nucleic acid sequence of claim 31 wherein the predicted free energy of folding is more positive than about -0.2 kcal/(mole)(base).

50. A method of designing a synthetic polynucleotide, the method comprising:

providing a starting polynucleotide;

determining the predicted free energy of folding per base of the starting polynucleotide;

modifying the starting polynucleotide by replacing at least one codon from the starting polynucleotide with a different codon to provide a modified polynucleotide;

determining the predicted free energy of folding per base of the modified polynucleotide; and

comparing the predicted free energy of folding of the modified polynucleotide with the predicted free energy of folding of the starting polynucleotide.

51. The method of claim 50 wherein the different codon corresponds to the same amino acid as the replaced codon.

52. The method of claim 50 further comprising:

(a) determining whether the predicted free energy of folding of the modified polynucleotide is changed relative to the predicted free energy of folding of the starting polynucleotide by a desired amount; and

(b) if the predicted free energy of folding of the modified polynucleotide is not changed by the desired amount, further modifying the modified polynucleotide by replacing at least one codon from the modified polynucleotide with a different corresponding codon to provide a different modified polynucleotide.

53. The method of claim 52 further comprising repeating steps (a) and (b) until the predicted free energy of folding of the modified polynucleotide is increased by the desired amount to ultimately provide a final polynucleotide.

54. The method of claim 52 wherein the desired free energy of folding of the modified polynucleotide is increased as compared to the predicted free energy of folding of the starting polynucleotide.

55. The method of claim 50 comprising physically creating the modified polynucleotide.

56. The method of claim 52 comprising physically creating the different modified polynucleotide.

57. The method of claim 53 comprising physically creating the final polynucleotide.

58. A synthetic polynucleotide designed by the method of claim 50.

59. A synthetic polynucleotide designed by the method of claim 52.

60. A synthetic polynucleotide designed by the method of claim 53.

61. A nucleic acid having one of the sequence of a polynucleotide designed by the method of claim 50 and a sequence complementary thereto.

62. A nucleic acid having one of the sequence of a polynucleotide designed by the method of claim 52 and a sequence complementary thereto.

63. A nucleic acid having one of the sequence of a polynucleotide designed by the method of claim 53 and a sequence complementary thereto.

64. The method of claim 50 wherein the codon replaced to make the modified polynucleotide corresponds to a different amino acid than was replaced in the starting polynucleotide.

65. The method of claim 50 wherein the different codon is selected from the most frequently used by a selected host.

66. The method of claim 52 wherein the starting polynucleotide is derived from a eukaryotic cell and is modified to be expressed in a selected prokaryotic host cell.

67. A method of physically creating a tangible synthetic polynucleotide comprising creating a physical embodiment of the synthetic polynucleotide of claim 58.

68. A method of physically creating a tangible synthetic polynucleotide comprising creating a physical embodiment of the synthetic polynucleotide of claim 59.

69. A method of physically creating a tangible synthetic polynucleotide comprising creating a physical embodiment of the synthetic polynucleotide of claim 60.

70. A physical embodiment of the tangible synthetic polynucleotide prepared by the method of claim 67.

71. A physical embodiment of the tangible synthetic polynucleotide prepared by the method of claim 68.

72. A physical embodiment of the tangible synthetic polynucleotide prepared by the method of claim 69.